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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/986,480 | 11/08/2001 | Craig A. Rosen | PS500P1 | 5616 |

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HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

| EXAMINER | |
|---|---|
| SHEINBERG, MONIKA B | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/986,480 | ROSEN ET AL. | |
| | Examiner | Art Unit | |
| | Monika B Sheinberg | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,8,13,15,17-21,23 and 25-56* is/are pending in the application.

4a) Of the above claim(s) *1,8,13,15,17-21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-56* is/are rejected.

7)☒ Claim(s) *30-35,41-47 and 52-55* is/are objected to.

8)☒ Claim(s) *1,8,13,15,17-21,23 and 25-56* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1 sheet* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *Detailed Action* .

## DETAILED ACTION

***Response to the Preliminary Amendment and Election filed: 17 April 2003***

***Election/Restrictions***

Applicant's election with traverse of Group III (claims 11, 12 and 16) and polypeptide sequence election of SEQ ID NO: 225; in the response filed: 17 April 2003, is acknowledged. The traversal is on the ground(s) that it would not be a serious search burden on the Examiner since "the searches for polynucleotides, polypeptides, antibodies, and methods of diagnosing and treating disease states using the proteins of the subject invention would clearly be overlapping" (p.11, 2nd paragraph). This is not found persuasive because the inventions are distinct for the reasons given in the previous Office action; they have acquired a separate status in the art because of their recognized divergent subject matter. The completely separate chemical types of the inventions of the nucleic acid, polypeptide, and antibody Groups supports the undue search burden if all were examined together.

The requirement is still deemed proper and is therefore made FINAL.

- The cancellation of claims 2-7, 9-12, 14, 16, 21 and 24; the amendments made to claims 1, 8, 13, 15, 17-21 and 23; and the addition of new claims 25-56, are acknowledged.
- Claims 1, 8, 13, 15, 17-21, 23 and 25-56 are pending.
- Claims 1, 8, 13, 15, 17-21 and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed: 17 April 2003.
- Claims 25-56, drawn to polypeptides as Group III, are hereby examined.

***Priority***

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. Support for the claims 25-56 are acknowledged in PCT/US00/12788 (5/11//2000) and the

provisional 60/134,068 (5/13/1999) with respect to SEQ ID NO: 225 and clone ID: HCUDW10 of this application. Priority date of the instant application is therefore considered to be May 15, 1999.

***Claim Rejections - 35 USC § 101/112***

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

- Claims 25-56 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well-established utility.

The claimed protein of claims 25-56 are not supported by a specific asserted utility because the disclosed uses of these compositions are not specific and are generally applicable to any predicted polypeptide sequence that was derived from computational analyses of the cDNA sequence. The computational analysis provided a predicted signal peptide and a predicted secreted peptide, yet no experimental characterization was performed for validation or support of the hypothesis. (Please note that the physical protein itself is not supported by the specification, all proteins/polypeptides are a mere translation of the nucleic acid sequence):

> In the present case, the deduced amino acid sequence of the secreted polypeptide was analyzed by a computer program called SignalP (Henrik Nielsen et al., Protein Engineering 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results shown in Table I. (p. 273)

> In the twelfth and thirteenth columns of Table 1, the first and last amino acid position of SEQ ID NO: Y of the predicted signal peptide is identified as 'First AA of Sig Pep" and Last AA of Sig Pep." In the fourteenth column, the predicted first amino acid, position of SEQ ID NO: Y of the secreted portion is identified as "Predicted First AA of Secreted Portion". The amino acid position SEQ ID NO: Y of the last amino acid encoded by the open reading frame is identified in the fifteenth column as Last AA of ORF" (p. 2)

The asserted specific utilities are based upon an analysis of the expression of nucleic acids in tissue distribution and not protein analysis. The cDNA itself is disclosed to potentially have errors.

> Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases). (p. 5, 2nd paragraph)

The nucleic acid sequence, SEQ ID NO: 65, from which the claimed polypeptide is translated from, consists 1302 base pairs. Thus an error in sequencing that is then translated may result in a silent point mutation thus retaining the intended amino acid; however other results may occur in

that a base that translates to a different amino acid of different characteristics (then fold changes) leads to a dysfunctional or completely non-functional protein; or a base that translates to a STOP codon prematurely terminates the full translation of a functional protein.

The claims as written encompass sequences that are sequences beyond exact identity (be it in entirety or to contiguous fragments) of the elected SEQ ID NO: 225. Absent factual evidence, a percentage sequence similarity of less than 100% identity or homology, is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known polypeptide. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results is an unpredictable and therefore unreliable correspondence between the claimed polypeptide and the indicated similar polypeptides of known function and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over polypeptides of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Attwood, T [*Science*, vol. 290, no. 5491, pp. 471-473 (2000)]; Gerhold et al. [*BioEssays*, vol. 18, no. 12, pp. 973-981(1996)]; Lopez et al. [*Molecular Biology*, vol. 32, pp. 881-891 (1999)]; Russell et al. [*Journal of Molecular Biology*, vol. 244, pp 332-350 (1994)]; and Wells et al. [*Journal of Leukocyte Biology*, vol. 61, no. 5, pp. 545-550 (1997)].

Further, it is unpredictable if the cDNA that encodes SEQ ID NO: 225 will successfully encode a functional protein in that it is not indicated to be a full-length open reading frame. Page 97 of the specification recites the utility of the protein encoded by Gene No. 55 (SEQ ID NO: 225) is for diagnosis and treatment of testicular cancer and associated metastases due to the gene being "expressed in testes and to a lesser extent in cDNA libraries derived from CD34 positive cells (cord blood), Soares melanocyte 2NbHM, normalized infant brain, fetal kidney, whole brain, and Merkel cells. It is noted that expression of an undisclosed amount in any of the above, was observed in cells not limited to the male reproductive system therefore the expression in testes

does not prove useful in diagnostic assays or treatment of testicular cancer. No characterization of the actual potential functional activity of the claimed protein is disclosed. Since there is no physical protein, the instant invention requires further experimentation to be able to have a protein from which further assays may be performed to determine and/or validate the actual function of the predicted peptide. The potential specific utility of the protein is determined by observation of an undefined level of gene expression difference in various non-specific tissues by nucleic acid analysis and not by protein analysis; no actual protein with a defined functionality or biological activity is disclosed thus there is no certainty of a useful isolated product.

> Biological Activities -
> The polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides or polypeptides, or agonists or antagonists could be used to treat the associated disease. Polynucleotides, translation products and antibodies corresponding to this gene may be useful for the diagnosis, prognosis, prevention, and/or treatment of diseases and/or disorders associated with the following systems. (p. 367)

The specification asserts that based on tissue distribution, the polypeptide compounds, and/or protein, may be useful in for diagnosis and treatment of testicular cancer and associated diseases. These associated diseases of the male reproductive system are in a laundry list from page 433 (line 31) to page 435 (line 10). The listed diseases and disorders described by the preferred indications of the polypeptide are non-specific, but covering a wide array of diseases and disorders. The laundry list of diseases or disorders that are encompassed within the above specified indications appear to cover an extremely broad range of disorders. Thus no specific use has actually been indicated as the preferred embodiment of SEQ ID NO: 225. In fact, the specification summarizes modern biotechnology generally (in the ability to utilize the claimed sequence for multiple assays of all sorts) but never connects the elected sequence to any particular or specific utility. This wishlist desire for a utility for the claimed sequence falls short of a readily available utility. Ideally, the use of examples in a given specification typically serve to demonstrate at least the critical limitations and/or requirements in order to make/use an invention. However, the examples are generic in nature and not specific to the elected sequence. The exemplary assays described within the specification are general to any disclosed polypeptide

and are non-specific uses that are applicable to proteins in general and not particular or specific to the polypeptide being claimed, SEQ ID NO: 225.

In addition, the protein is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The protein is only slightly characterized by results of tissue distribution based upon a general expression analysis. The research contemplated by applicant(s) to characterize potential protein products, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities such as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the protein compound(s) such that another non-asserted utility would be well established for the compounds.

- Claims 25-56 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility, or, alternatively, a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

- Claims 25-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
    - WRITTEN DESCRIPTION: Claims 25-56 are directed to a predicted polypeptide sequence. Applicants have not experimentally isolated the claimed 'isolated protein', but merely base the description on homology and predictive analyses such as the region of amino acids that may carry characteristics such as signal peptide and secreted peptide.

In addition, the claims are directed to encompass proteins corresponding to sequences of 90% or 95% identity to the overall of SEQ ID NO: 225. The specific 10% or 5% that are not identical to the elected sequence are represented by the claim are not supported by the specification. Although the sequence itself distinguishes the structural features of the nucleic

acid, sequences, beyond exact identity (be it in entirety or to contiguous fragments) of the elected SEQ ID NO: 225, are included but not disclosed as to written description. Each variation of the 5% or 10% non-identical, results in a new and independent sequence that does not reliably result in similar or identical biological activities as result for example from altered folding patterns. For example, it would have been known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. As discussed above, in the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Thus the instant claims are directed to encompass peptide sequences that correspond to sequences from other species, mutated fragment sequences, allelic variants, splice variants, and so forth. None of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

- WRITTEN DESCRIPTION: Claims 31-36, 42-46 and 52-56 are directed to biological deposits. See MPEP 2400:

> The deposit rules (37 CFR 1.801 - 1.809) set forth examining procedures and conditions of deposit which must be satisfied in the event a deposit is required. The rules do not address the substantive issue of whether a deposit is required under any particular set of facts.

Examiner has tried to review the specification for support that demonstrates compliance to the deposit rules, however has been unsuccessful. Applicant is requested to point to the pages that provided the required information showing that compliance has been met. If the deposit is not in accordance with the regulations, the claims do not meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the biological deposits of the claims. Please refer to the biological deposit rules 37 CFR 1.801 - 1.809.

***Claim Objections***

Claims 31-36, 42-46 and 52-56 are objected to due to the claims not further limiting the subject matter of claims 25-30, 37-41 and 47-51 respectively. As disclosed by the specification

the polypeptide SEQ ID NO: 225 correlates directly to the HCUDW10 cDNA contained in ATCC Deposit No. 209197, thus it is unclear what are the differences in the metes and bounds of the parameters covered by claim 25 and claim 31 for example. Claim 25 requires the isolated protein to include amino acid residues 31-198 of SEQ ID NO: 225; these residues are indicated in Table 1 (p. 259) to be the 'secreted portion' of the peptide that corresponds to HCUDW10 cDNA: ATCC Deposit No. 209197. Claim 31 requires "the amino acid sequence of the secreted portion of the polypeptide encoded by the HCUDW10 cDNA contained in ATCC Deposit No. 209197"(lines 1-3). Thus the requirements of for example claims 31-36 are the literal translation of the limitations numerically and succinctly described in claims 25-30.

***Conclusion***

- Claims 25-56 are rejected under 35 U.S.C. 101/112 – utility.
- Claims 25-56 are rejected under 35 U.S.C. 112, first paragraph – written description.
- Claims 30-35, 41-47 and 52-55 are rejected under 35 U.S.C. 112, first paragraph – written description, biological deposit.
- Claims 30-35, 41-47 and 52-55 are objected.

No claim is allowed.

***Inquiries***

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Souaya, can be reached at 703-308-6565. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 6, 2003

Monika B. Sheinberg
Art Unit 1634

MBS

JEHANNE SOUAYA
~~PATENT~~ EXAMINER
Primary

Jehanne Souaya
Aug. 7, 2003